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RESEARCH ARTICLE

Effects of Polyphenol-rich Cornelian Cherry (*Cornus mas* L.) and Barberry (*Berberis vulgaris*) Fruits Extract on Reducing *in vitro* Starch Digestibility: An Evaluation of Hydrolysis Index

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HIGHLIGHTS

- The amount of rapidly digestible starch was decreased by the treatments of barberry extract and cornelian cherry extract and the hydrolysis index of white bread was also decreased.
- Barberry has more inhibitory effects on α-amylase activity than cornelian cherry.
- Dietary polyphenols such as anthocyanins and catechins found in cornelian cherry and barberry fruit reduce starch digestion by inhibiting α-amylase and α-glucosidase.

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ABSTRACT

The purpose of this study was to investigate the polyphenol-rich cornelian cherry (*Cornus mas* L.) and barberry (*Berberis vulgaris*) fruits extract on reducing the *in vitro* starch digestibility of white bread and evaluation of glycemic indexes. When we evaluated the association between the Rapidly digestible starch (RDS) and Hydrolysis index (HI), the amount of RDS was decreased by the treatments of barberry extract and cornelian cherry extract and the HI of white bread was also decreased. It is thought that the barberry has more inhibitory effects on α-amylase activity than cornelian cherry. We also demonstrated that dietary polyphenols such as anthocyanins and catechins found in cornelian cherry and barberry fruit reduced starch digestion by inhibiting α-amylase and α-glucosidase. When we compare the RDS, SDS, and RS values between the cornelian cherry and barberry treatments, the barberry treatment on WB showed a better-quality starch fraction than the cornelian cherry treatment. This may be because the barberry has a higher amount of antioxidant capacity than the cornelian cherry. Generally, two berry fruits had the effect of reducing the starch digestibility of WB. Thus, consumption of colored berries may contribute to reducing the GI of foods. These findings are demonstrating that barberry and cornelian cherry consumption is favorable for the dietary management of metabolic disorders such as diabetes and hyperlipidemia. According to the results of this study, functional products can be developed to control blood glucose in diabetes. There is a need for more comprehensive studies on this subject that will reveal the causes of the problem.

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1. Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetes mellitus is the most common metabolic disease with an increasing number of newly diagnosed patients. This disease is a global health problem and has a huge impact on health systems [1]. The 9th edition of the Diabetes Atlas by the International Diabetes Federation estimates that the prevalence of diabetes will increase from 425 million worldwide in 2017 to 629 million by 2045 [2]. Nutrition has a central place in diabetes management with its clear impact on weight and metabolic control. Medical nutrition therapy offers an evidence-based approach to diabetes management through lifestyle changes that are highly recommended prior to initiating pharmaceutical therapy. Therefore, it is crucial to identify and implement effective dietary strategies to treat hyperglycemia and prevent the progression of diabetes through dietary and lifestyle changes [3]. Carbohydrate intake is a precursor to the elevation of blood glucose. Therefore, controlling the amount and quality of carbohydrates used is critical in diabetes and obesity management. Foods containing carbohydrates are used as energy sources throughout the world. However, the risk of diabetes and its optimal amount are still controversial. In addition, attention has been drawn to the quality of carbohydrates, as the absorption rates and elevated blood sugar levels of foods containing carbohydrates differ. Even with the same amount of carbohydrates in the food, the satiety effect of rising blood sugar varies from one food to another. These variations are meant to grow glycemic index concepts. The glycemic index (GI) is an *in vivo* measure of the relative effect of carbohydrate-containing foods on postprandial blood sugar [4]. Numerous studies have been designed to better investigate their interactions with other components of the food matrix, such as carbohydrates, dietary fiber, proteins and/or lipids, resulting in modulation of the bio-availability/bio-accessibility of polyphenols during digestion [5]. In particular, the bio-availability/bio-accessibility of phenolic compounds seems to depend on several factors such as their molecular structure, the complexity of the phenolic-carbohydrate superstructure, and the catalytic activity of enzymes on carbohydrates. In contrast, unreleased (chemically bound) polyphenols may potentially positively affect the human body as they can reach the large intestine, where local enzymatic and microbial activities increase their bio-accessibility [6]. Therefore, the aim of this study was to evaluate the use of polyphenol-rich barberry and cranberry fruit extracts in modulating glucose release from carbohydrate foods, white bread, under *in vitro* simulated digestion conditions.

2. Materials and Methods

2.1. Materials

Methanol, ethanol, potassium hydroxide (KOH), sodium acetate, pepsin (from porcine gastric mucosa, 250U/mL), pancreatin (from porcine pancreas, 8×USP specifications), and guar gum were obtained from Sigma-Aldrich Co., LLC. (St. Louis, MO, USA). Invertase (from yeast, 300U/mL), thermostable α-amylase (from *Bacillus licheniformis*, 3000U/mL), amyloglucosidase (from *aspergillus niger*, 3330U/mL), and glucose oxidase-peroxidase (GOPOD) reagent were purchased from Megazyme (Wicklow, Ireland).

2.2. Sampling

Barberry and cornelian cherry fruits, which were used as research material, were collected about 1 kilogram from the mountainous land in August 2020 from the Pınarbaşı district of Kastamonu and kept in ice boxes and appropriate containers and taken to the Nutrition and Dietetics Department R&D laboratories, where the first stage of our study was carried out. It was stored in a deep freezer at -80°C until analysis. The consultancy was received from the Kastamonu Provincial Directorate of Agriculture and Forestry for the distribution of barberry and cornelian cherry fruits in mountainous areas (Table 1).

Table 1 Harvest date of fruit samples and the region where they were harvested

Fruit name	Harvest date	Assembly area
Cornelian cherry	26.08.2020	Kastamonu, Pınarbaşı highland
Barberry	30.08.2020	Kastamonu, Pınarbaşı highland

2.3. Starch Analysis

Determination of starch content of white bread was found with some modifications in the method of Goñi et al. [7]. First, 0.1g of white bread was weighed into a 50 mL falcon tube and treated with 0.2mL of aqueous ethanol (80%, v/v) to induce dispersion. Next, 2mL of KOH (2M) solution was added and mixed with a magnetic stick (5 x 15mm) for 10 minutes in an ice/water bath. Then, 8 mL of sodium acetate (1M) solution (pH 3.8) was added. Thermostable α-amylase

and amyloglucosidase (0.1mL) enzymes were added to initiate starch hydrolysis. The reaction was carried out at 50°C for 30 minutes. The final volume of the hydrolyzed solution was made up with deionized water and centrifuged at 8000rpm for 5 minutes. After this step, 0.1mL of centrifuged liquid sample was treated with 3.0mL of GOPOD solution in a 10 mL glass tube in a water bath at 50°C for 30 min. Its absorbance at 510nm was measured using a UV spectrophotometer (UV-1280, Shimadzu).

2.4. *In vitro* Starch Digestibility and Predicted Glycemic Index

In vitro starch digestibility of polyphenol-rich cranberry *(Cornus mas L.)* and barberry *(Berberis vulgaris)* fruit extracts treated with white bread was measured using the method of Englyst et al. [8] with some modifications. Gastric and intestinal enzymes for digestion were prepared as follows.

Enzyme Solution 1 (Pepsin/Guar Gum Solution): 0.5g pepsin and 0.5g guar gum were dissolved in a 0.05N HCl solution in a 100ml measuring flask. The final volume was made up with 0.05N HCl. Enzyme Solution 2 (pancreatin (136mg/mL), amyloglucosidase (13.4 U/mL) and invertase (25.43U/mL) for one sample): For a sample, 680mg pancreatin 4 mL deionized water in a 50ml falcon tube. Then it was centrifuged at 3000rpm for 10 minutes and the residue was discarded 67U of amyloglucosidase and 127.15U of invertase were then added to the centrifuged pancreatin fluid sample and the volume was made up to 5ml with deionized water.

2.5. *In vitro* Starch Digestibility

In this study, each polyphenol-rich cornelian cherry *(Cornus mas L.)* and barberry *(Berberis vulgaris)* fruits extracts were treated with 1g homogenized white bread in 250ml Erlenmeyer flask. Digestion was started by adding 5mL of deionized water and 10mL of Enzyme Solution 1. The mixture was incubated at 37°C in a shaking water bath (175 strokes/min) for 30 min for protein hydrolysis. Then 5.0mL of sodium acetate solution (0.5M) was added, and the pH was adjusted to 5.2. After this step, Enzyme Solution 2 (5 mL) was added and the volume was made up to 50mL with deionized water and incubated at 37°C in a shaking water bath. During the incubation, 0.5 mL of liquid sample was taken at 20, 30, 60, 90, and 120 min and transferred into a 10 mL glass tube. The solution was kept in a boiling water bath for 5 minutes to complete the denaturation of the digestive enzymes. The liquid sample was transferred to a 15mL falcon tube and the volume was made up to 5mL and then centrifuged at 8000rpm for 10 minutes. Finally, the glucose content was measured as in the starch determination.

The starch fractions were determined as follows:
Rapidly digestible starch (RDS) is defined as the starch digested in 20 minutes. Slowly digestible starch (SDS) is defined as the starch digested in between 20 and 120 minutes.

$$Resistant\ starch\ (RS) = TS - (RDS + SDS) \quad (1)$$

$$Total\ starch\ (TS) = TG \times 0.9 \quad (2)$$

3. Results

3.1. Starch Fractions

In this study, the effects of polyphenol-rich cornelian cherry *(Cornus mas L.)* and barberry *(Berberis vulgaris)* fruits extracts on the amount of RDS, SDS, and RS in White bread (WB) were investigated, and results are shown in Table 2. RDS is defined as the starch digested in 20 min. When comparing WB treated with barberry and WB treated with cornelian cherry; the amounts of RDS in barberry-treated WB was higher, but the highest amounts of RDS was in non-treated WB. SDS is defined as the starch digested in between 20- and 120-min. When comparing WB treated with barberry and WB treated with cornelian cherry; the amounts of SDS in cornelian cherry-treated WB was higher, but the highest amounts of SDS was in non-treated WB. RS is defined as the difference between the total starch and the amount of starch digested within 120 min. A higher amount of RS was detected in WB treated with barberry while the lower amount was detected in WB treated with cornelian cherry.

The ratio of starch digestion levels of WB treated with different extracts from the initial starch digestion to 120 min is shown in Graphic 2. A lower starch digestion ratio was detected in the WB treated with cornelian cherry by 10.0% at 20 min. On the other hand, the higher ratio at 20 min was detected in the WB treated with barberry by 10.2%. The WB treated with barberry showed the lowest starch digestion (27.5%) compared with non-treated WB (36.7%) at 120 min.

3.2. Hydrolysis Index

The HI of the WB treated with extracts was calculated by comparing the area under the hydrolysis curve (0 to 120 min) from WB treated with herbal extracts to the area of non-treated WB (i.e. the reference sample). The hydrolysis curves for the WB treated with different extracts are shown in Figure 1.

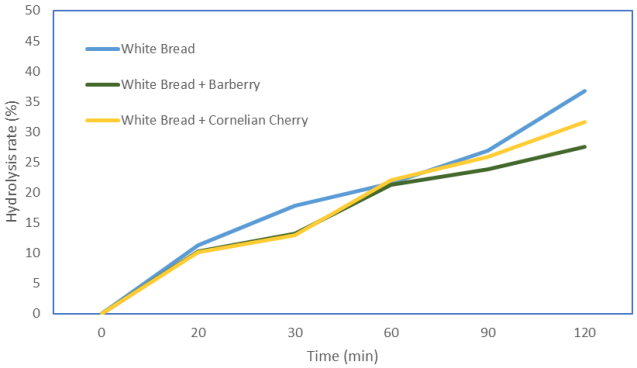

Figure 1 White bread, barberry, and cornelian cherry hydrolysis rate according to time

Calculated HI values of the WB treated with different extracts are shown in Table 2. The HI of the WB treated with different extracts ranged from 86 (barberry) to 92 (cornelian cherry). As seen, the WB treated with different extracts showed lower HI than the non-treated WB. When we compared the effects of different extracts on the HI of WB, treatment with barberry the HI of WB more than cornelian cherry.

Table 2 Fruit extracts and white bread HI, RDS, SDS, RS and TS values

	White Bread	White Bread + Barberry	White Bread + Cornelian Cherry
HI	100±4a	86±3b	92±3c
RDS	5.369±0.188a	4.881±0.171b	4.800±0.168c
SDS	12.121±0.424a	8.126±0.288b	10.250±0.359c
RS	30.100±1.054a	34.493±0.207b	32.451±1.139c
TS	47.591±1.666	47.591±1.666	47.591±1.665

When we evaluated the association between the RDS and HI, the amount of RDS was decreased by the treatments of barberry extract and cornelian cherry extract and the HI of white bread was also decreased. The amount of RS was increased by the treatments with barberry extract and cornelian cherry extract while the HI of white bread was decreased. Treated barberry and cranberry extracts decreased the HI of WB while increasing the RS level compared to non-treated WB.

4. Discussion

Variation in the ability of carbohydrates to increase blood glucose is captured by the glycemic index, which ranks carbohydrate foods according to their blood-glucose raising ability. Dietary GI is a measure of the overall ability of consumed carbohydrates to raise blood glucose [9]. It was reported that a low-GI diet, containing foods with carbohydrates that are more slowly digested and absorbed than a high GI diet, can normalize glucose excursions. Also, this type of diet is now recommended as part of dietary management in both Type 1 (T1DM) and Type 2 Diabetes Mellitus (T2DM) [10]. The starch in WB is composed of amylose and amylopectin fractions. The main enzymes that play a role in the digestion of dietary starch are α-amylase and α-glucosidase [11]. It was found that generally the inhibitory activity of flavonoids against a-amylase enhanced with the molecular hydroxylation at hydrogen atom positions, because the hydroxyl group is able to interact with amino acid residues at the active sites of the enzyme [12]. The foods containing dietary polyphenols such as anthocyanins, catechins, flavanones, flavonols, flavones, and isoflavones may reduce carbohydrate digestion by inhibiting α-amylase and α-glucosidase in the small intestine [11]. The cornelian cherry *(Cornus mas L.)* from the family of *Cornaceae* is a kind of traditional plant grown frequently in the past in many countries in traditional cuisine and folk medicine [13]. Medicinal benefits from cornelian cherry fruits are attributed to the polyphenols and iridoids among which loganic acid and cornuside as well as anthocyanins of cyanidin, delphinidin and pelar-gonidin are the most dominant [14]. Popović et al. studied the active compounds of *Cornus mas L.* demonstrated the antidiabetic and antioxidant effects via the attenuation of hyperglycemia and inhibition of oxidative modifications of proteins and lipids, advanced glycation and oxidation protein formation or accumulation. It is thought in that study that cornelian cherries can be considered as a food supplement to alleviate diabetes mellitus and its complications [15]. As seen from our study, cornelian cherry treatment decreased both the RDS and SDS levels and HI of WB and increased the RS level compared with non-treated WB.

Berry products contain distinguished polyphenol constituents. The Berry fruits family is rich in polyphenols such as procyanidins, quercetin, phenolic acids, and especially anthocyanins. *Berberis vulgaris*, commonly known as barberry, is a berry fruit with high polyphenol content. The barberry fruits have a sour taste and contain malic acid, tartaric acid, and citric acid. The barberry's fruits, flowers, and seeds contain significant amounts of phenolic compounds, including anthocyanin and carotenoid pigments, pectin, oleoresin, vitamin C, and organic acids such as chelidonic acid, resin, and tannin [16]. The medicinal use of the fruits of B. vulgaris in the literature is lacking, but there are many other traditional uses cited for the other parts of the plant, but they are not the object of this study. Regarding the chemical composition of barberry fruits, the scientific data shows that they contain little or no alkaloids. However, they contain a great amount of phenolics, gum, pectin, oleoresins, and organic acids. Several pharmacological effects have been demonstrated for the barberry fruit extract. Among these are cytoprotective and antioxidant actions and anticholinergic and anti-histaminergic effects [17]. Previous studies have shown that barberry is used to treat liver disease, depression, hyperlipidemia, and hyperglycemia. The results of clinical trials on the effect of barberry on glycemic indices have been inconsistent; some studies have shown beneficial effects of barberry on glycemic indices, while in some studies, barberry has a lesser or negative effect on these indices [18, 19]. Safari et al. [20] studied that suggests that although barberry supplementation significantly improves insulin levels; however, other glycemic indices might not be affected. As seen from our study, barberry treatment decreased both the RDS and SDS levels and HI of WB and increased the RS level compared with non-treated WB. It is thought that the barberry has more inhibitory effects on α-amylase activity than cornelian cherry. Thus, cornelian cherry treatment on white bread produced a further effect on the HI of white bread compared with barberry.

5. Conclusion

It has been hypothesized that high glycemic index foods promote fat storage and increase the risk of obesity. The intake of lower GI foods provides significant benefits over those with a higher GI, as it produces less drastic metabolic and hormonal changes, facilitates the return of glucose levels to basal levels, creates a greater feeling of satiety, and then creates a greater feeling of fullness. The literature also provides evidence that polyphenol-rich diets, containing phenolic compounds, have been shown to exhibit remedial benefits by ameliorating insulin secretion and insulin resistance. In the present study, we demonstrated that dietary polyphenols found in cornelian cherry and barberry could reduce starch digestion by the inhibition of α-amylase and α-glucosidase resulting in lowering the HI of foods. When we compare the RDS, SDS, and RS values between the cornelian cherry and barberry treatments, the barberry treatment on WB showed a better-quality starch fraction than the cornelian cherry treatment. This may be because the barberry has a higher amount of antioxidant capacity than the cornelian cherry. Generally, two berry fruits had the effect of

reducing the starch digestibility of WB. Thus, consumption of colored berries may contribute to reducing the GI of foods.

Declaration of Conflict of Interest

Authors declare that they have no conflict of interest with any person, institution, or company.

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